REMARKS

Claims 28 to 30 and 37 to 39 are all the claims pending in the application.

The present invention as set forth in claim 28 is directed to a method for reducing fatigue in animals in the state of fatigue, wherein the animals are middle aged or older persons and wherein the fatigue is physical exhaustion, which comprises administering a composition containing reduced coenzyme Q.

Applicants have relied on the Examples of the present specification to show unexpected results to overcome the rejection of the claims under 35 U.S.C. § 103(a) as obvious over WO 2002/092067 to Fuji et al in view of the Wilson et al publication, and further in view of the excerpt from Remington's Pharmaceutical Sciences (Fifteenth Edition, 1980, page 712)..

In the Advisory Action of August 25, 2009, the Examiner states that these Examples do not establish unexpected results.

With respect to Example 1, the Examiner states that Example 1 does not demonstrate any unexpectedly greater effect using "reduced coenzyme Q10" versus "oxidized CoQ10" because the total concentration of coenzyme Q that appears in the muscle using reduced CoO10 versus oxidized CoQ10 versus the control all fall within the standard deviation of one another.

However, it appears that the Examiner may not understand the meaning of the results shown in Table 1 of the present application, which Table 1 was amended in the Amendment filed on October 19, 2009, for Example 1 and Comparative Example 1.

In particular, Table 1 shows that results for the reduced coenzyme Q group (Example 1) were statistically significant as compared to the control group (described in Example 1), but that

the results of the oxidized coenzyme Q (Comparative Example 1) were not statistically significant as compared to the control group.

With respect to the Examiner' argument that the total concentrations of coenzyme Q that appear in the muscle using reduced CoQ10 versus oxidized CoQ10 fall within the standard deviation of one another and, thus do not demonstrate any unexpectedly greater effect for reduced coenzyme Q, applicants point out that experimental data obtained using animal models inevitably shows varied widely. Therefore, the obtained numerical data is statistically processed taking into consideration the average and standard deviation and evaluated objectively.

As can be seen from Table 1, in Comparative Example 1, a significant increase in the level of coenzyme Q in muscle was not confirmed by the administration of oxidized coenzyme Q10. On the contrary, as can be seen from Table 1, in Example 1, a significant increase was statistically confirmed by the administration of reduced coenzyme Q10.

Thus, the presence of a significant difference based on the objective statistical processing establishes a superior effect of reduced coenzyme Q.

With respect to Example 2, the Examiner states in the Advisory Action that while reduced coenzyme Q10 demonstrated a greater concentration in the muscle versus the control or oxidized CoQ10, this would have been reasonably expected because reduced coenzyme Q10 was the agent actually being administered and, thus, would have been expected to result in a greater concentration in the muscle.

In response, applicants point out that Table 2 shows that the total coenzyme Q significantly decreased when employing oxidized coenzyme Q as compared to the control,

whereas the total coenzyme Q significantly increased when employing reduced coenzyme Q as compared to the control. Applicants submit that this is an unexpected result.

Oxidized coenzyme Q is conventionally known to be reduced to become reduced coenzyme Q in the body.

Conversely, however, the level of reduced coenzyme Q10 in muscle decreased by the administration of oxidized coenzyme Q10 and increased by the administration of reduced coenzyme Q, as shown in Table 2. Therefore, the present invention provides an unexpected effect.

Applicants note that "Total CoQ" in the last column of Table 2 means a total of reduced coenzyme Q (reduced coenzyme Q10 + reduced coenzyme Q9), rather than a total of coenzyme Q (oxidized coenzyme Q10 + reduced coenzyme Q10).

Examples 1 and 2 reveal remarkable effects that the total coenzyme Q (reduced coenzyme Q + oxidized coenzyme Q) (Table 1) and total reduced coenzyme Q (Table 2) increase by the administration of reduced coenzyme Q, as compared to the administration of oxidized coenzyme Q.

With respect to Example 3, the Examiner states in the Advisory Action that while it has been demonstrated that the reduced coenzyme Q10 or oxidized coenzyme Q10 prolonged maximum running time via reducing fatigue, it is noted that the tested rats were "young rats" and not "middle aged or older rats" as instantly claimed and that the combination of reduced and oxidized CoQ10 (to which some of the instant claims are directed) was never tested.

With respect to Example 4, the Examiner states in the Advisory Action that the combination of reduced and oxidized CoQ10 (to which some of the instant claims are directed) was never tested.

In response, applicants submit that the Examiner has not correctly analyzed the results of Examples 3 and 4, and that he, therefore, comes to the wrong conclusion when he points out that Example 3 is directed to young rats, and not middle aged or older rats. Further, the Examiner does not provide any comments on whether the specific results in Example 4 are unexpected.

In particular, with respect to Example 3, and the Examiner's comment that the tested rats were young rats, and not middle aged or older rats, applicants are not relying on Example 3 to show that the results in Example 3 were unexpected.

Instead, Example 3 provides a comparison with Example 4 in which aged rats were tested. Example 3 and Comparative Example 3 together show that in young rats, oxidized coenzyme Q and reduced coenzyme Q each has a significant prolongation effect on the maximum running time. One of ordinary skill in the art, therefore, would expect that the action of reduced coenzyme Q in aged rats would be the same as the action of oxidized coenzyme Q in aged rats.

Contrary to this expectation, Example 4 and Comparative Example 4 show that reduced coenzyme Q had a significant prolongation effect on the maximum running time of aged rats, but that oxidized coenzyme Q showed no or only a slight prolongation effect on the maximum running time of aged rats. Comparative Example 4 states that oxidized coenzyme Q had a poor efficacy for aged rats. In view of the fact that Example 3 and Comparative Example 3 showed

the same effect in young rats, one of ordinary skill in the art would expect that reduced coenzyme Q when used in aged rats would have the same effect as oxidized coenzyme Q in aged rats, but Example 4 shows that the effect of reduced coenzyme Q in aged rats is significantly better than oxidized coenzyme Q in aged rats. This is an unexpected result on which the Examiner has not made any comment.

Thus, Example 3 is presented for comparison with Example 4, and Examples 3 and 4 in combination demonstrate a remarkable fatigue reducing effect for middle aged or older persons.

Example 4 employed "aged" rats of 61 to 63 weeks. The present claims are directed to middle aged and older persons. From age-life span relationship between human and rat, 60-week-old rats approximately correspond to humans in their 30's. However, in terms of activity amount, 60- week-old rats are of the level of humans in their 50's and 60's. Accordingly, 61- to 63-week-old rats used in Example 4 correspond to 60-year old humans, i.e., (middle aged or) older persons.

With respect to the Examiner's comment that the combination of reduced coenzyme Q and oxidized coenzyme Q was never tested, applicants point out that the reduced coenzyme Q in Examples 3 and 4, in fact, was a combination of reduced coenzyme Q and oxidized coenzyme Q. Thus, the reduced coenzyme Q in these examples contained 1% oxidized coenzyme Q.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

Sheldon I. Landsman

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Sheldon I. Landsman
Registration No. 25,430

Date: January 20, 2010